AP Presentation

Part of combinatorial chemistry

* It is a collection of techniques for the synthesis of arrays or libraries of related chemical entities
* Relies extensively on encoding and decoding strategies for identification of active compounds

Coding Strategies

* Fall into two broad categories
  + Strategy one
    - Whole library is synthesized as pools of compounds
    - After assay we obtain active pools which are smaller than the original pool that are further solved into the active compound or we get discrete compounds
  + Strategy two
    - A different new compound is chemically synthesized on a resin bead
    - Assay are then performed with either the compound still on the bead or with the compound cleaved but the relationship with the bead is retained
    - The active compound is then identified by reading a code on the bead via direct sequencing
* Mass encoding falls under the second category

What is Mass encoding

* Mass spectrometry has been used to identify compounds from a single bead, i.e., those used in library synthesis
* The sensitivity of the instrument is a limiting factor when using bead that are very small 10 micro meter
* In principle any number of codes can be generated, it is ideal to reduce the number of these, as well as the chemical investment
* Mass encoding further has different types of reading these so called “codes”
* Single peak positional encoding
  + As the name implies MS in this case gives a single peak is generated for each distinct code
  + In this Link 2 is cleaved to allowed the compound to be tested for activity and when the compound tests positive the link 1 is cleaved and the code block is submitted for MS
* Double peak positional encoding
  + In this the code block is prepared in the same way but has 2 species
  + One is reference mass and the other is the code block of the single peak positional variable peaks
  + The advantage of this over single peak is that the code can be left attached to the ligand and read at the same time as the mass of the whole construct
* Bar code
  + Requires use of mixed isotopically distinct code monomers at each step of code synthesis
  + These are present in equal concentrations and hence the individual reactivity is not affected by isotopic composition
* Ratio code
  + This is a very different strategy than the ones described previously
  + Can be implemented on the level of a single atom, code can be conveniently inserted whenever a common reagent which is used at a single compound or ligand